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Aplastic Anemia as the Sole Presentation of Systemic Lupus Erythematosus

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INTRODUCTION

Hematologic abnormalities such as anemia of chronic disease, hemolytic anemia, leukopenia, and immune thrombocytopenia are found in up to 59% of patients with systemic lupus erythematosus (SLE) over the course of their disease [1,2]. In contrast, disorders of the bone marrow such as pure red cell aplasia or myelofibrosis are extremely rare in SLE and are not considered part of the diagnostic criteria for the disease [2–4].

Although mild cytopenias are common in SLE, rarely are blood dyscrasias the sole presenting feature of the disease in the absence of other clinical criteria [1,2]. We describe two new cases of systemic lupus erythematosus in which aplastic anemia and pancytopenia were the sole manifestations of the disease months prior to other clinical features. The interval from the onset of pancytopenia to the diagnosis of SLE ranged from 3 to 12 months.

CASE 1

A 33-year-old asymptomatic Hispanic male was referred for pancytopenia. The complete blood count revealed a leukocyte count of 2.8×10^9/L (nl 4.0–10.0 $\times$ 10^9/L), hemoglobin 11.5 g/dL (nl 14.0–18.0 g/dL), and platelet count 96×10^9/L (nl 150–450 $\times$ 10^9/L). Bone marrow biopsy revealed hypocellularity without fibrosis (90% fat, 10% cell) (Fig. 1A). Serum obtained from the patient was added to normal hematopoietic precursor cells in culture and failed to inhibit CD 34+ stem cells, Burst forming unit-erythroid (BFU-E), or Colony forming unit-granulocyte monocyte (CFU-GM) in vitro.

The patient remained asymptomatic over the next 12 months with persistent pancytopenia. Subsequently, he developed a discoid lupus rash and arthralgias. Further evaluation demonstrated a positive anti-nuclear antibody (ANA), anti-double stranded DNA, anti-Smith antibody, and urinary protein of 800 mg/24 hr. A diagnosis of SLE was made and plaquenil 200 mg twice daily was begun. The rash and arthralgias resolved and the pancytopenia improved within 2 months. Most recent complete blood count showed a leukocyte count of 3.7×10^9/L, hemoglobin 13.3 gd/L, and platelet count 149×10^9/L.

CASE 2

A 35-year-old female was referred for evaluation of fever and pancytopenia. Initially, her leukocyte count was 0.4×10^9/L, hemoglobin 8.6 g/dL, and platelet count 99×10^9/L. A complete work up for infections, including HIV serology, was negative. Bone marrow biopsy demonstrated hypocellularity (80% fat, 20% cell), and no evidence of leukemia (Fig. 1B). T-cell lymphocyte predominance was also identified in the bone marrow aspirate by immunophenotypic analysis. The lymphocytes were CD 7 positive (early T cell antigen) and lacked CD 10, 19, and 20 (B cell antigens). Serum obtained from the patient

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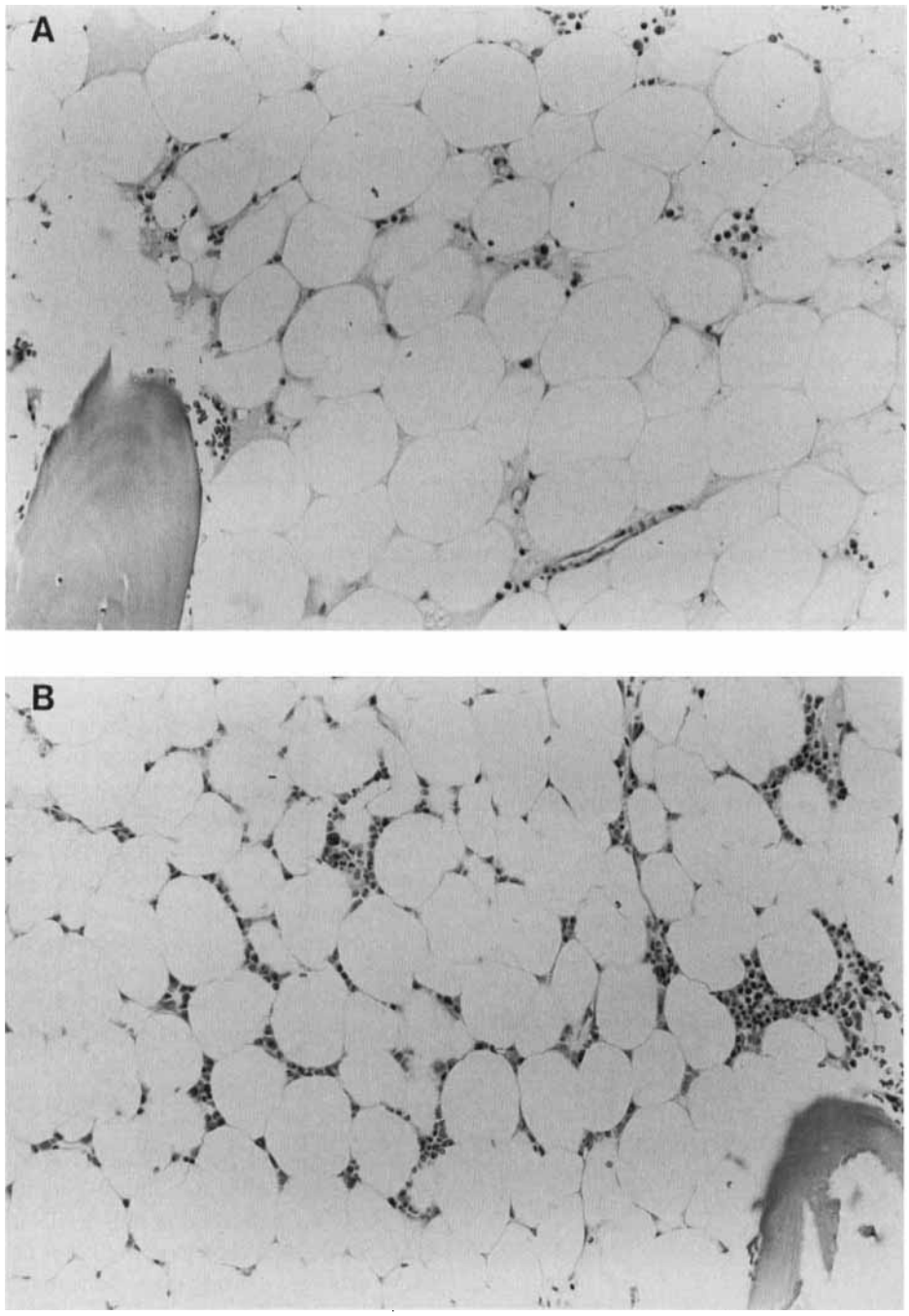

Fig. 1. Bone marrow biopsies. A: Patient 1: Bone marrow biopsy demonstrating severe aplasia (Hematoxylin & Eosin, ×20). B: Patient 2: Severe aplasia (H & E, ×20).

at diagnosis failed to inhibit the growth of normal CD 34+ stem cells, BFU-E, or CFU-GM in vitro. ANA, anti-double stranded DNA, anti-Smith antibodies, and a Coombs test were initially negative.

Three months later, the patient developed a malar rash, proteinuria (1.2 g/24 hr), and a positive anti-phospholipid antibody test. The ANA (1:320 speckled pattern) and the anti-Smith antibody became positive. SLE was diagnosed and the patient was started on prednisone, 1 mg/kg/day. One month later, the leukocyte count was 8.0×10^9/L, hemoglobin 13.2 g/dL, platelet count 205×10^9/L, and the rash and fevers resolved.

DISCUSSION

The patients described in this series are unusual because in each case, aplastic anemia was the presenting feature of systemic lupus erythematosus and the pancyto-

penia predated other more typical clinical manifestations of SLE by 3 to 12 months. Failure of multiple hematologic cell lines as the presenting feature of SLE has not been previously described [1,5,6].

Aplastic anemia and myelofibrosis have been reported in association with fulminant cases of SLE, but these are exceedingly rare events, occurring much less commonly than peripheral autoantibody induced cytopenias [2,7]. Previously, it has been postulated that a serum inhibitor may be responsible for suppression of normal stem cell and colony forming unit proliferation in patients with aplastic anemia [8]. Our investigations failed to demonstrate a serum inhibitor which could suppress bone marrow elements. Serum obtained at diagnosis in both patients did not inhibit CD 34+ stem cells, CFU-GM, or BFU-E cells in culture.

It has also been proposed that T cell dysregulation may mediate the suppression of normal hematopoiesis in patients with SLE [9]. In our series, patient 2 demonstrated T cell predominance by immunophenotypic analysis in the bone marrow. In-vitro models have suggested that soluble mediators of T cell function such as interferon-gamma or tumor necrosis factor-alpha may contribute to the bone marrow suppression seen in patients with aplastic anemia [10]. The demonstration of aplasia and T cell proliferation in patient 2 suggests that T cell dysfunction may have contributed to the development of aplasia in this patient.

Analysis of our patients and review of the medical literature demonstrates that the pathogenesis of pancytopenia in SLE is not uniform. T cell dysregulation, serum inhibition of hematopoietic elements, and peripheral autoantibody production all may contribute to the final clinical picture. Our experience suggests that aplastic anemia and pancytopenia may occur as the presenting feature of systemic lupus erythematosus more commonly than previously described. Pancytopenia may be evident and severe for several months prior to any other signs of the disease. In patients who present with aplasia and pancytopenia, the diagnosis of systemic lupus erythematosus should be included in the differential. Oral high dose prednisone is rapidly effective in correcting the pancytopenia when it occurs.

REFERENCES

1. Nossent JC, Swaak AJG: Prevalence and significance of haematological abnormalities in patients with systemic lupus erythematosus. Quart J Med 80:605–612, 1991.
2. Kneeling DM, Isenberg DA: Haematological Manifestations of Systemic Lupus Erythematosus. Blood Rev 7:199–207, 1993.
3. Tan EM, Cohen AS, Fries JF, et al.: The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 25:1271–1277, 1982.
4. Inoue Y, Matsubara A, et al.: Myelofibrosis and systemic lupus erythematosus: Reversal of fibrosis with high-dose corticosteroid therapy. Acta Haematol 88:32–36, 1992.
5. Videbaek A: Auto-immune haemolytic anaemia in systemic lupus erythematosus. Acta Medica Scand 171:187–194, 1962.
6. Rabinowitz Y, Damesheck W: Systemic lupus erythematosus after idiopathic thrombocytopaenic purpura, a review: A study of systemic lupus erythematosus occurring after 78 splenectomies for idiopathic thrombocytopaenia purpura, with a review of the pertinent literature. Ann Intern Med 52:1–28, 1960.
7. Cavalcant J, Shadduck R, et al.: Red-cell hypoplasia and increased bone marrow reticulin in systemic lupus erythematosus: Reversal with corticosteroid therapy. Am J Haematol 5:253–263, 1973.
8. Brooks BJ Jr, Broxmeyer HE, Bryan CF, Leech SH. Serum inhibitor in systemic lupus erythematosus associated with aplastic anemia. Arch Intern Med 144:1474, 1984.
9. Sumimoto S, Kawai M, Kasajima Y, and Hamamoto T: Aplastic anemia associated with systemic lupus erythematosus. Am J Hematol 329–331, 1991.
10. Miura A, Endo K, Sugawara T, Kameoka J, et al.: T cell mediated inhibition of erythropoiesis in aplastic anemia: The possible role of IFN-gamma and TNF-alpha. Br J Haematol 3:442–449, 1991.